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Abstract

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Grant Number: 1R01DA014339-01
PI Name: CARELLI, REGINA M.
PI Email: rcarelli@unc.edu
PI Title:
Project Title: Neurophysiological Study: Cocaine & Natural Reinforcers

Abstract: Numerous investigations indicate that the nucleus accumbens (Acb) is crucially involved in mediating the reinforcing actions of drugs of abuse such as cocaine and `natural' reinforcers such as food and water. We recently completed a series of studies that examined the activity of the same Acb neurons in rats responding on multiple schedules for either two distinct `natural' reinforcers (water and food), or one of those `natural' reinforcers and the intravenous self-administration of cocaine (Carelli et al., 2000; Appendix D). The results showed that the majority of neurons tested exhibited similar, overlapping neuronal firing patterns across the two `natural' reinforcer conditions. In contrast, the majority of neurons examined (> 90%) exhibited differential, nonoverlapping firing patterns relative to operant responding for water (or food) vs. cocaine reinforcement. Given these findings, four experiments are proposed in this application to provide critical information regarding factors that influence and/or control Acb reinforcement-related cell firing in behaving animals. Exp. 1 will determine the anatomic distribution of neurons in the Acb that selectively encode information related to water vs. cocaine reinforcement. This will be accomplished by the strategic positioning of microelectrodes into the core, shell and/or rostral pole of the Acb, and the specific `marking' of wires from which reinforcer selective cell firing was recorded during a water/cocaine multiple schedule. Exp. 2 will extend that study and determine if reinforcer selective cell firing is apparent during initial exposure to cocaine or if it is a direct consequence of repeated self-administration experience. Information gained in those studies will be expanded in Exps. 3 & 4 by determining the effects of interruption of drug access (abstinence) on cocaine selective cell firing. This is a critical issue since cocaine addiction in humans is typically characterized by periods of abstinence from drug taking and relapse (Gawin, 1991; O'Brien et al., 1992). Specifically, Exp. 3 will determine the firing properties of Acb neurons following various periods of cocaine abstinence (2, 4 and 8 weeks). Exp. 4 will determine the effects of cocaine abstinence on the associative properties of Acb cell firing documented in a number of published reports by the PI. Results of Exp. 4 will be directly relevant to understanding the biological basis of stimulus control in cocaine addiction reported to be a major contributor to problems in human drug abusers (O'Brien et al., 1992; Childress et al., 1999). Collectively, these studies will provide important insight into the functional organization of the Acb and its role in reinforcement-related processing

in behaving animals.

Thesaurus Terms:
cocaine, neurophysiology, reinforcer
brain mapping, drug /alcohol abstinence, neuroanatomy, neuron, nucleus accumbens, water drinking behavior
electrophysiology, laboratory rat, microelectrode

Institution:	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL CHAPEL HILL, NC 27514
Fiscal Year:	2001
Department:	PSYCHOLOGY
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Grant Number: 1R21DA014962-01
PI Name: CARELLI, REGINA M.
PI Email: rcarelli@unc.edu
PI Title:
Project Title: Combined Voltammetry/Electrophysiology in Behaving Rats

Abstract: DESCRIPTION: (provided by the applicant) This application is written in response to the Program Announcement entitled, "Cutting Edge Basic Research Awards" (PA #: PAR-01-047) designed to foster 'high-risk and potentially high-impact' research that will 'advance our understanding of drug abuse and addiction'. The PI has completed a number of electrophysiological recording experiments in behaving rats to investigate underlying cellular mechanisms mediating the reinforcing properties of cocaine as well as 'natural' (water/food) reinforcement. One advantage of this approach is that it enables the characterization of nucleus accumbens (Acb) cell firing at critical times during goal-directed behaviors. For example, the PI and others have shown that a subset of Acb neurons appear to encode the 'critical' features of drug or appetitive reinforced responding including response initiation, response execution and reinforcement delivery (e.g. Bowman, et al., 1996; Schultz et al., 1992, Carelli and Deadwyler, 1994, 1997; Carelli et al., 2000; Peoples et al., 1997, 1998; Chang et al., 1994, 1998). However, one disadvantage of this approach is that the role of dopamine (DA) in reward-related processing can only be indirectly inferred in electrophysiology experiments. In contrast, fast scan cyclic voltammetry can be used to directly measure DA in the Acb on a millisecond time scale with micron spatial resolution that provides chemical information analogous to that obtained from electrophysiological unit recording. In this regard, the PI is currently working in collaboration with Dr. Mark Wightman, an analytical chemist and pioneer in the development and application of this technique in behaving animals, to examine changes in DA efflux in the Acb during cocaine self-administration sessions in rats. The purpose of this proposal is to expand those studies and to measure changes in Acb cell firing and Acb dopamine from the same electrode in behaving rats. Specifically, Aim 1 will develop the technology for combined electrophysiological recording and voltammetric measurements of DA in the Acb from the same electrode in awake rats. Aim 2 will expand that study and apply this technology to examine Acb cell firing and corresponding changes in DA levels in the Acb during cocaine self-administration sessions in rats. This combined electrophysiology/voltammetry approach will provide the first unique view of real-time, spatially resolved concentration fluctuations of DA in conjunction with changes in cell firing in the Acb during goal-directed behaviors. As such, we will be able to directly examine the contribution of DA in mediating underlying

cellular mechanisms in the Acb that are involved in encoding information related to cocaine reinforcement.

Thesaurus Terms:
brain electrical activity, cocaine, dopamine, electrical measurement, electrophysiology, goal oriented behavior, technology /technique development
drug abuse, drug addiction, nucleus accumbens, operant conditioning, self medication
behavioral /social science research tag, electrode, histochemistry /cytochemistry, laboratory rat

Institution:	UNIVERSITY OF NORTH CAROLINA CHAPEL HILL CHAPEL HILL, NC 27514
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